

Cell Biology

POTENTIATION OF MURINE IMMUNITY BY ANTIFUNGAL DRUGS

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Many studies have shown that antifungal antibiotics are able to profoundly enhance host immune response. Among these antibiotics is the polyene antifungal molecule Amphotericin B (Fungizone, Squibb) influencing immune parameters including delayed type hypersensitivity (DTH) to contact sensitizing chemicals and polyclonal B cell activation. Recently we have been examining the ability of an imidazole antifungal molecule Fluconazole (Diflucan, Pfizer) to effect murine DTH to the chemical sensitizing agent dinitrofluorobenzene (DNFB; Sigma) using an ear-thickness assay. Briefly DNFB was applied to the shaved abdomens of groups of AKR/J mice on day 0 and 1 of the assay, with varying dosages of fluconazole or saline (controls) also administered intraperitoneally on day 0 and 1; on day 13 the right ear thickness of each mouse was individually determined, ear painting with DNFB done, and subsequent ear thickness measurements done at 24 hour intervals. Fluconazole boosted DTH response to DNFB at 1.0, 2.0, 4.0 and 6.0 mg total dosages compared to saline controls. Fluconazole alone with no abdominal DNFB exposure showed no enhancement of DTH response. Optimal fluconazole dosage and time frame for fluconazole exposure relative to DNFB exposure and magnitude of DTH response was determined. Fluconazole also was found to reverse tolerization of mice to DNFB by intravenous injection of 2,4-dinitrobenzenesulfonic acid sodium salt DNBSO₃ (Kodak). These effects of fluconazole on murine DTH appear to be due to effects on T cell function, and should correlate with efficacy of fluconazole treatment in patients with fungal infections.